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LETTER

Detection vs. selection: integration of genetic, epigenetic and environmental cues in fluctuating environments

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Abstract

There are many inputs during development that influence an organism's fit to current or upcoming environments. These include genetic effects, transgenerational epigenetic influences, environmental cues and developmental noise, which are rarely investigated in the same formal framework. We study an analytically tractable evolutionary model, in which cues are integrated to determine mature phenotypes in fluctuating environments. Environmental cues received during development and by the mother as an adult act as detection-based (individually observed) cues. The mother's phenotype and a quantitative genetic effect act as selection-based cues (they correlate with environmental states after selection). We specify when such cues are complementary and tend to be used together, and when using the most informative cue will predominate. Thus, we extend recent analyses of the evolutionary implications of subsets of these effects by providing a general diagnosis of the conditions under which detection and selection-based influences on development are likely to evolve and coexist.

Keywords

Adaptive development, bet hedging, habitat tracking, maternal effects, plasticity, reaction norm, transgenerational effects.

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INTRODUCTION

Organisms are sensitive to a variety of inputs during development, often producing phenotypes that are suited to current or upcoming environments (West-Eberhard 2003). Adaptive phenotypic plasticity and transgenerational effects are among the well-studied examples. In spatially varying environments, genetic variation contributes to local adaptation (e.g. Levene 1953; Seger & Brockmann 1987; Kawecki & Ebert 2004) and allele frequencies will vary spatially. An individual's genotype will therefore statistically contain information about local environmental conditions and thus can be regarded as a genetic cue that can be combined and integrated with environmental and transgenerational cues adaptively during development (Lively 1986; Sultan & Spencer 2002; Leimar *et al*. 2006; Dall *et al*. 2015; Leimar & McNamara 2015). In temporally fluctuating environments on the other hand, it is traditional to consider only environmental cues and, sometimes, transgenerational cues as being the developmental influences that fit phenotypes to current conditions. Random phenotype determination (diversified bet hedging) is another important adaptation to unpredictable environments (Seger & Brockmann 1987). Both evolutionary modelling (Lachmann & Jablonka 1996) and empirical observation (Bergland *et al*. 2014; Cogni *et al*. 2015) indicate that genetic variation plays a role in fitting phenotypes to temporal environmental variation, provided that the time scale of variation is longer than the generation time of the organism. However, such genetic effects are rarely investigated alongside trangenerational effects, bet hedging and adaptive plasticity in the same formal framework. Here we study the relative importance and interaction of all of these influences on phenotype determination in temporally varying environments, using an evolutionary model that, to a great extent, can be worked out analytically.

Amongst transgenerational epigenetic effects, Shea *et al*. (2011) make the distinction between *detection-based* and *selection-based* effects. The former are concerned with the influence of cues about environmental conditions that are directly observed and are passed down the generations. Indeed, current environmental influences on adaptive development can also be thought of as detection-based effects (equivalent to information by 'instruction': Jablonka & Lamb (2005)). In contrast, selection-based effects do not require direct observations by individuals. They occur when there is transmission (with reasonable fidelity) of an epigenetic marker down successive generations, where the marker affects the phenotype, and so is under selection, and as a result of past selection current individuals tend to adaptively match their environment. Such selection-based effects (via heritable genetic variation) also form the basis of the 'genes-as-cues' analysis of Leimar *et al*. (2006) and Leimar & McNamara (2015) in spatially heterogeneous environments. Here, for the first time, we explore the relative value of using the full range of potential detection-based and selection-based cues during development

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in temporally varying environments in the same model. In environments without spatial structure, it is only favourable for the parental generation to pass information to offspring when environments are autocorrelated (so that knowledge of the environment in one year is predictive of the environment in the following year) (Shea *et al.* 2011; Kuijper *et al.* 2014; English *et al.* 2015; Kuijper & Hoyle 2015; Uller *et al.* 2015). In this case, the maternal phenotype or cue genes can act as selection-based sources of information, and this is the situation we study.

In our model there are two environmental sources of information (Fig. 1) that act as direct detection-based cues; during development each individual receives a cue of the current environment ('juvenile cue') that can affect the adult phenotype; in addition each individual receives a further environmental cue as an adult that can be passed to offspring. Both cues are subject to noise and so are not perfectly informative. There are also two selection-based cues; the phenotype of the mother and a quantitative genetic effect, present in the offspring, that, in our model acts as a cue to the offspring, but can also be seen as a breeding value for the trait in question. The phenotype of an individual can depend on its juvenile cue, its mother's phenotype, the mother's adult cue and its inherited quantitative genetic cue genes, as well as developmental noise, the level of which is under selection (Fig. 1). As in Rivoire & Leibler (2014), our analysis involves two different timescales; the environment, the distribution of maternal phenotypes and that of the genetic cue genes all vary from

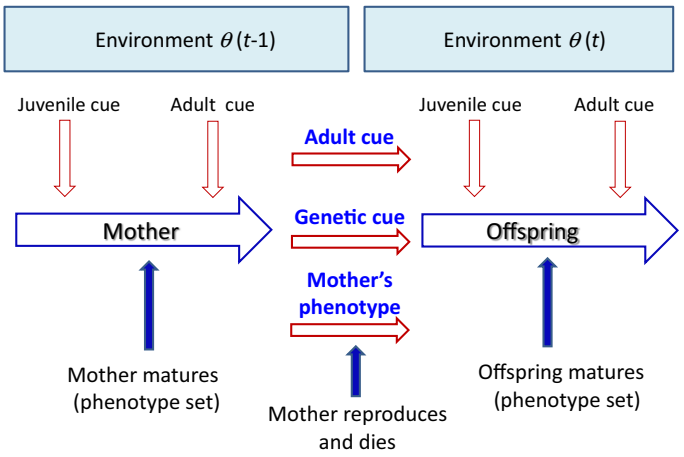

Figure 1 Phenotype determination of an individual in generation t. In generation $t-1$, the mother receives a juvenile environmental cue during development and then matures, at which time her phenotype is set. Her reproductive success is a function of this phenotype and the current environmental state. She also receives a further environmental cue as an adult. This cue does not affect her phenotype, which is already set but is passed on to the offspring in generation t, along with the information about her phenotype and her mutated cue genes. These three cues, together with an environmental cue received as a juvenile, determine the phenotype of the offspring. There are thus two detection-based cues; the adult maternal environmental cue and the juvenile environmental cue, and two selection-based cues; the maternal phenotype and cue genes. Note that if phenotypes are influenced by environmental cues, the mother's phenotype as a cue will combine elements of detection and selection (see text).

generation to generation, whereas the developmental system that integrates these cues is passed on to offspring without error. We seek the developmental system that maximises the long-term growth rate in the number of individuals that employ this means of phenotype determination.

It has been previously suggested that the use of a genetic cue determines its correlation with the environment and hence value as a cue (Leimar 2009); a use it or lose it principle. For the first time, we give an explicit demonstration of this principle. However, our main focus is on the interaction of the various cues, and how this interaction depends on the rate of environmental change and the accuracy of cues and information transmission. Some previous models (Rivoire & Leibler 2014; English *et al.* 2015; Leimar & McNamara 2015) have considered combinations of cues, but our model, which considers a specific purely temporarily varying environment, allows an analytic expression for fitness and is, we believe, particularly suited to exposing the logic of cue integration. Unlike Rivoire & Leibler (2014), we allow separate inheritance channels so as to have a clear separation and analysis of the effects of selection-based versus detection-based cues, which are otherwise entangled. Although the synergy between detection and selection-based cues has been previously proposed (e.g. Kuijper & Hoyle 2015), we give the first clear demonstration of the positive synergy between environmental cues and the maternal phenotype; the combination of these cues results in much higher fitness than when only one of these cues is used. In contrast, environmental cues and cue genes do not synergise in the same way and incorporating both does not always result in higher fitness. Thus, unlike recent models that analyse the evolutionary implications of subsets of cues (e.g. Leimar *et al.* 2006; Shea *et al.* 2011; Kuijper *et al.* 2014; Kuijper & Hoyle 2015; Leimar & McNamara 2015; Kuijper & Johnstone 2016) our analysis provides a general diagnosis of the conditions under which detection and selection-based influences on development are likely to evolve and/or coexist.

METHODS

We assume an asexual population with discrete, non-overlapping generations. There are two genetically determined elements. One is a quantitative effect that acts as a genetic cue to the developmental system. The other is the cue integration system itself. This system determines how the genetic cue, maternal phenotype, two types of environmental cues and noise jointly influence development and hence determine the adult phenotype. We allow the quantitative genetic trait to evolve for a given cue integration system, finding the fitness of the cue integration system. We then find the cue integration system with the greatest fitness. Model details are similar to that of Rivoire & Leibler (2014). Both models allow the influence of detection-based cues to be inherited (a form of Lamarckism) but in Rivoire & Leibler (2014), the mother passes a single quantity on to her offspring. This quantity is a linear combination of the maternal phenotype, the cue received by the mother as an adult and the quantity passed on to the mother by her mother. In contrast, we allow for the maternal phenotype, the adult maternal cue and the genetic

cue genes to be passed on to offspring separately before the offspring combines them to determine its phenotype (Fig. 1).

The environment

The environmental state in generation t is $\theta(t)$. The dynamics are given by

$$\theta(t+1) = \lambda\theta(t) + \epsilon_\theta(t). \quad (1)$$

Here $0 < \lambda < 1$ and $\epsilon_\theta(t) \sim N(0, \sigma^2)$ is independent of current and previous environmental states. The stochastic process $\{\theta(t);\ t = 0, 1, 2, \ldots\}$ is then a stationary Markov process with an equilibrium distribution that is normally distributed with mean 0 and variance

$$\mathrm{Var}(\theta) = \frac{\sigma^2}{1-\lambda^2}. \quad (2)$$

The parameter λ is the correlation coefficient between environmental states at successive times; i.e.

$$\rho(\theta(t+1), \theta(t)) = \lambda. \quad (3)$$

The genetic cue

The quantitative genetic effect can take any real value. Surviving offspring of a parent with genetic effect value z' have effect value $z = z' + \epsilon_Z$, where $\epsilon_Z \sim N(0, \sigma^2_{mut})$.

Environmental cues

A juvenile in generation t receives two environmental cues that can affect its mature phenotype; it observes the juvenile cue C_J (where $C_J \sim N(\theta(t), \sigma_J^2)$) and is passed the cue C_A (where $C_A \sim N(\theta(t-1), \sigma_A^2)$) that its mother observed as an adult (Fig. 1). These cues are conditionally independent given these environmental states. Within a generation, the cues received by different population members are also conditionally independent resulting in a distribution of cues that is centred on the current environmental state. This distribution varies across generations as the environment varies.

Phenotype determination

The adult phenotype of an individual is given by

$$x = \alpha z + \beta_J c_J + \beta_A c_A + \gamma(m + \epsilon_m) + \delta\epsilon_\delta, \quad (4)$$

where z is the value of its genetic effect, c_J is its juvenile environmental cue, c_A is the adult environmental cue observed by her mother, m is the phenotype of the mother, $\epsilon_m \sim N(0, \sigma_m^2)$ is the error in transmission of the maternal phenotype to the offspring and $\epsilon_\delta \sim N(0, 1)$ is a developmental noise term. Here α, β_J, β_A, γ and δ are non-negative genetically determined parameters that specify the action of the developmental system.

Reproductive success

Reproductive success is a function of the fit of the phenotype to the environment; specifically an individual of phenotype x leaves

$$Ke^{-\frac{1}{2}(x-\theta)^2} \quad (5)$$

surviving offspring when the environmental state is θ. Here K is a positive constant.

Fitness

We evaluate the geometric mean fitness $G(\alpha, \beta_J, \beta_A, \gamma, \delta)$ of the developmental system. Consider a large (essentially infinite) cohort of individuals with this developmental system. Let $X(t)$ be the phenotype of a randomly selected cohort member and $\bar{X}(t)$ the mean phenotype in generation t. We show (Supporting Information, Section SI.1) that if within a generation the joint distribution of $X(t)$ and the quantitative genetic effect are bivariate normal then they remain so in future generations. We thus assume that the distribution of $X(t)$ given $\bar{X}(t) = \bar{x}$ is normal with mean $\bar{x}$ and variance σ_X^2. We also argue (SI.2) that this variance tends to a limiting stationary value, and we assume the cohort has achieved this value. Let $\theta(t) = \theta$ and $\bar{X}(t) = \bar{x}$. Then, since the cohort is large (so that we can average over demographic stochasticity), between generation t and $t+1$ the cohort grows by the factor

$$R(\theta, \bar{x}) = K\mathbb{E}(e^{-\frac{1}{2}(X(t)-\theta(t))^2} | \theta, \bar{x}). \quad (6)$$

Thus, using the fact that the conditional distribution of $X(t)$ is normal we have

$$R(\theta, \bar{x}) = \frac{K}{\sqrt{1+\sigma_X^2}} e^{-\frac{1}{2}\frac{(\bar{x}-\theta)^2}{1+\sigma_X^2}}. \quad (7)$$

The geometric mean fitness of the developmental system is

$$G(\alpha, \beta_J, \beta_A, \gamma, \delta) = e^{\mathbb{E}(\ln R(\theta, \bar{X}))}, \quad (8)$$

where the expectation is taken with the respect to the stationary distribution of the vector process $\{(\theta(t), \bar{X}(t)) :\ t = 0, 1, 2, \ldots\}$. Since $\bar{X} - \theta$ is symmetric about zero, and hence has mean 0 (SI.4) we have $\mathbb{E}((\bar{X}-\theta)^2) = \mathrm{Var}(\bar{X}-\theta)$. Thus

$$G(\alpha, \beta_J, \beta_A, \gamma, \delta) = \frac{K}{\sqrt{1+\sigma_X^2}} \exp\left[-\frac{1}{2}\frac{\mathrm{Var}(\bar{X}-\theta)}{1+\sigma_X^2}\right]. \quad (9)$$

Note that fitness depends on the weights α, β_J, β_A, γ, δ through their influence on both σ_X and $\mathrm{Var}(\bar{X}-\theta)$. We denote the values of these weights that maximise fitness by α^*, β_J^*, β_A^*, γ^*, δ^*.

RESULTS

Diversified bet hedging

Suppose that individuals receive no information on the current environmental state ($\alpha = \beta_J = \beta_A = \gamma = 0$) so that the phenotype determination is given by $x = \delta\epsilon_\delta$. Then the best fixed trait value is $x = 0$ since the environment is symmetric about $\theta = 0$. However, always maturing with this phenotype is not a robust strategy when the environmental variance is

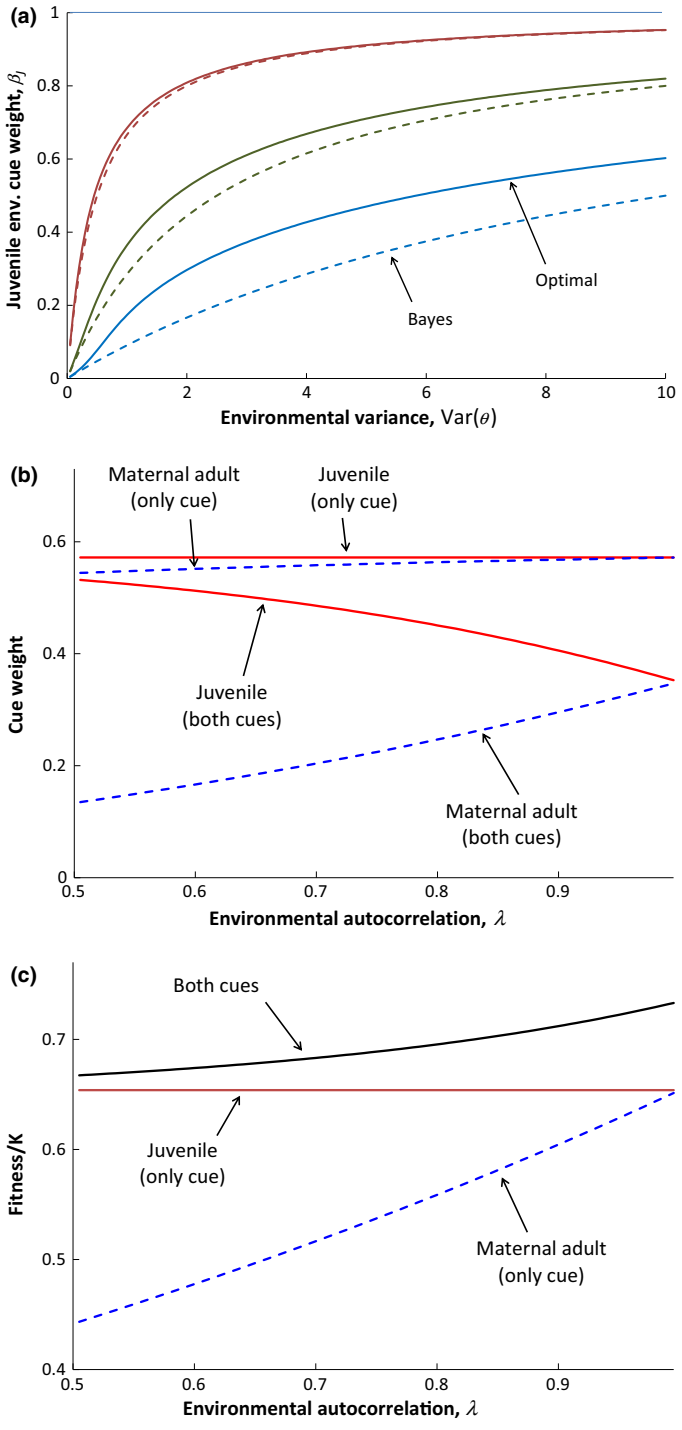

Figure 2 Individuals may receive one or both of two environmental cues; a juvenile cue during development and a cue passed on from the mother that the mother received as an adult. (a) Effect of the environmental variance when individuals receive only a juvenile cue. Solid curve: the optimal juvenile cue weight β_J^* for three value of the juvenile cue error variance (top curve $\sigma_J^2 = 0.5$, middle curve $\sigma_J^2 = 2.5$, bottom curve $\sigma_J^2 = 10$). Dashed curve below the corresponding solid curve: the value β_{bayes} such that $\beta_{bayes}c_J$ is the Bayes posterior mean for θ given the cue c_J. (Note that β_J^* is the same for all combinations of the values of σ^2 and λ that result in the same value of Var(θ); this result can be derived from the formulae in SI.4.) (b) Effect of the environmental autocorrelation on optimal cue weights. Top two curves: individuals receive just one of the cues. Bottom two curves: individuals receive both cues. (β_J^* solid curve, β_A^* dashed curve.) (c) Effect of the environmental autocorrelation on fitness of the optimal developmental system when only the adult cue to the mother is available (bottom curve), only the juvenile cue is available (middle curve) and both cues are available (top curve). In (b) and (c), cue error variances $\sigma_J^2 = \sigma_A^2 = 2.5$, and as λ increases σ is decreased so that the environmental variance if held fixed at the value Var(θ) = 2.5.

large, and a strategy that incorporates diversified bet hedging will achieve greater geometric mean fitness (cf. Seger & Brockmann 1987). Specifically, in SI.5, it is shown that the optimal phenotype determination is given by $x = \delta^*\epsilon_\delta$, where $\delta^* = 0$ for Var(θ) < 1 and $\delta^* = \sqrt{\text{Var}(\theta) - 1}$ for Var(θ) ≥ 1.

Environmental cue during development

Suppose juveniles receive a cue during development, but no other cue so that $x = \beta_J c_J + \delta\epsilon_\delta$. Since different individuals receive different cues (whose distribution centres on the underlying environmental state), producing a range of phenotypes within a generation, the need to have additional diversified bet hedging is removed and $\delta^* = 0$ (SI.6). Thus, we can restrict attention to phenotype determination of the form $x = \beta_J c_J$.

Two values of β_J have an obvious statistical interpretation. $\beta_J = 1$ corresponds to using the minimum variance unbiased estimator for θ. This estimator has mean θ for all θ but has high variance within a generation. The arithmetic mean (over θ) annual growth in genotype numbers is maximised by setting $\beta_J = \beta_{bayes}$, where $\beta_{bayes} = \text{Var}(\theta)/(\text{Var}(\theta) + \sigma_J^2)$ is the Bayes posterior mean for θ given cue c_J. This method of phenotype determination results in a large discrepancy between the mean phenotype within a generation and θ when $|\theta|$ is large, and consequently has a high variance in annual growth. As Fig. 2a illustrates the optimal value of β_J is a compromise between these two values; i.e. $\beta_{bayes} < \beta_J^* < 1$ (See SI.6 for a proof).

Environmental cue received by the mother as an adult

If an individual's only cue is that which is experienced by its mother as an adult (i.e. $x = \beta_A c_A$), the value of this cue depends on the likely change in the environment between the maternal and the current generation. As a result, the optimal weight put on this cue increases with increasing environmental autocorrelation λ (Fig. 2b).

When an individual receives both adult maternal and juvenile cues during development ($x = \beta_J c_J + \beta_A c_A$), it can be shown that $\beta_J^* + \lambda\beta_A^* < 1$ (SI.8). Since the juvenile cue is more up to date, more weight should be placed on it when both cues have the same cue error variance; although as the environmental autocorrelation increases to its maximum value of 1, the weights become equal (Fig. 2b). Similar effects of the degree of environmental stability were obtained by English *et al.* (2015) and Leimar & McNamara (2015). As can be seen from Fig. 2c, in this example, the juvenile cue is more important in terms of fitness than the maternal adult cue when λ is low. Both cues contribute significantly to fitness for high environmental autocorrelation.

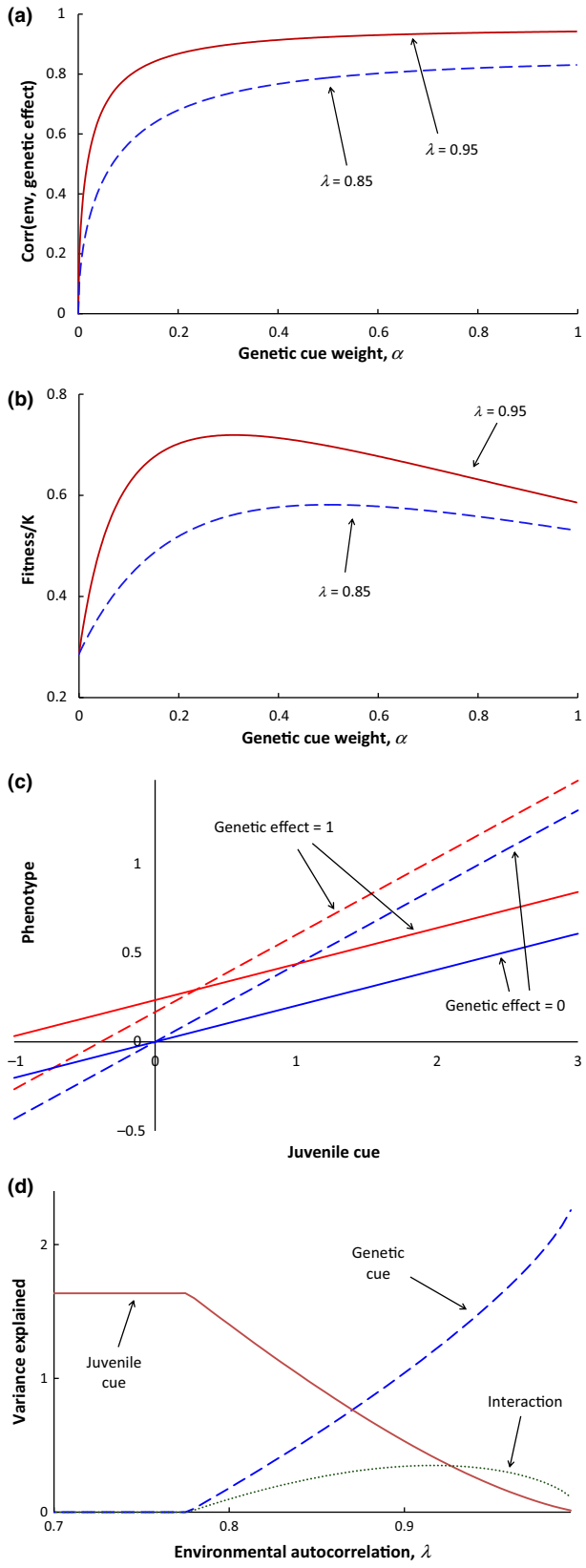

Figure 3 Quantitative genetic effect as a cue. (a) Correlation between the genetic effect and the environmental state (taken across individuals and generations) when there are no other cues. Solid curve $\lambda = 0.95$, dashed curve $\lambda = 0.85$. Mutation variance $\sigma^2_{mut} = 1.0$. (Correlations derived from the formulae in SI.4.) (b) Fitness of the developmental system for the cases considered in (a). (c) Optimal norms of reaction to the juvenile cue ($x = \alpha^* z + \beta^*_J c_J$) for two values of the genetic effect (blue, genetic effect $z = 0$; red, genetic effect $z = 1$), shown for two values of the environmental autocorrelation (solid curves, $\lambda = 0.95$; dashed curves, $\lambda = 0.85$). (d) Breakdown of the total phenotypic variance (both within and across generations) under optimal phenotype determination. Solid curve: variation explained by response to the juvenile cue ($(\beta^*_J)^2\sigma^2_J$), dashed curve: variation explained by response to the genetic effect ($(\alpha^*)^2 \mathrm{Var}(Z)$), dotted curve: variation explained by the interaction between these cues ($2\alpha^*\beta^*_J Cov(Z, C_J)$). (Here Z and C_J are the genetic effect value and juvenile cue value, respectively, of a randomly selected population member in a random generation.) In all cases σ is chosen so that $\mathrm{Var}(\theta) = 2.5$.

Genetic cue

Suppose that the quantitative genetic effect is the only available cue and there is no randomisation, so that phenotype determination is given by $x = \alpha z$. If this cue is ignored ($\alpha = 0$), there is no selection on the genetic effect and its value is uninformative. As α increases, the selection pressure on the genetic effect increases resulting in an increased correlation between the effect and the environmental state (Fig. 3a) so that the effect acts as a selection-based source of information. In other words, the more notice is taken of the genetic effect, the more informative is its value, leading to a feedback in which it should be used more. This feedback is limited; fitness declines for high α (Fig. 3b) since too high a value leads to too much variation in the phenotype within a generation (high σ^2_X, cf. eqn 9).

As the environmental autocorrelation increases for a given $\mathrm{Var}(\theta)$, so that the environment varies more slowly but has the same variability, selection leads to a higher correlation between the genetic effect and the environmental state (Fig. 3a), leading to an increase in fitness (Fig. 3b). This is in contrast to the effect of λ for a purely juvenile cue.

Regardless of what combination of cues is available, the fitness of the optimal developmental system does not depend on the mutation rate of the effect genes since an increase in the mutation rate is equivalent to a proportionate decrease in the parameter α; fitness depends on α and σ_{mut} only through the product $\alpha\sigma_{mut}$. (This can be deduced from SI.2 to SI.4.) When there is just the genetic cue, it may be optimal to have some randomisation ($\delta^* > 0$). The range of environmental parameters for which randomisation is optimal is explored in Rivoire & Leibler (2014).

Figure 3c,d illustrates optimal phenotype determination when there is both a genetic and a juvenile cue. In this case, no additional randomisation is required ($\delta^* = 0$). Fig. 3c illustrates the optimal norm of reaction to the juvenile cue for two values of the genetic effect. As can be seen, the slope of the norm of reaction is less and influence of the genetic effect is stronger when the environmental autocorrelation is higher. Fig. 3d shows the amount of phenotypic variation that is attributed to the influence of each cue. (Since fitness depends on the parameter α only through $\alpha\sigma_{mut}$, in presenting results, we have shown the breakdown of total variance rather than showing α^*.) For low values of the environmental autocorrelation λ, the genetic cue is not used even though this cue would have been used had the juvenile cue not been available,

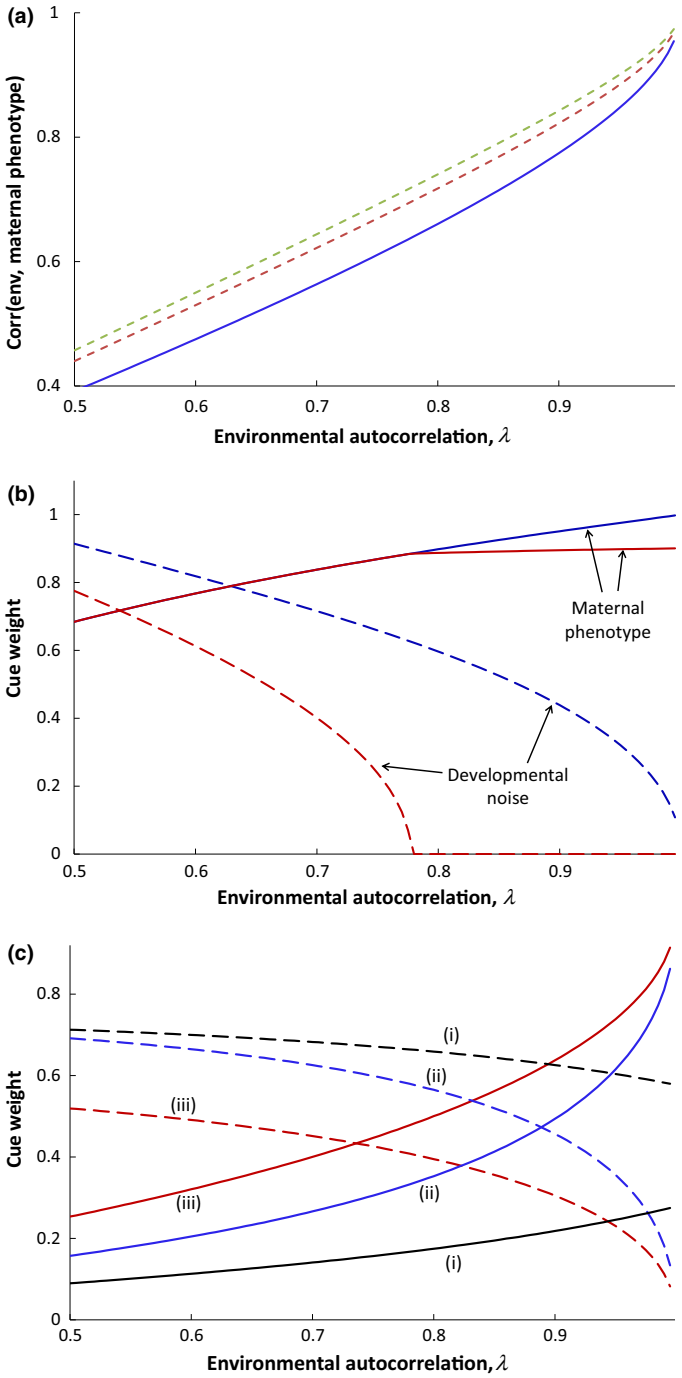

Figure 4 The maternal phenotype as a cue. (a) Correlation between the maternal phenotype and the current environmental state under optimal phenotype determination. Solid curve: when there is no other cue but developmental noise is allowed (so that the phenotype is determined as $x = \gamma^* m + \delta^* \epsilon_\delta$). Dashed curves: when in addition there is also a juvenile cue during development (top dashed curve $\sigma_J^2 = 1.0$, lower dashed curve $\sigma_J^2 = 2.5$. Transmission of maternal phenotype information is error free ($\sigma_m^2 = 0$). (b) Optimal phenotype determination when maternal phenotype is the only cue and there is developmental noise. Solid curve: the weight given to the maternal phenotype γ^*. Dashed curve: the amount of randomisation δ^*. In each case the upper (blue) curve corresponds to transmission of the maternal phenotype without error ($\sigma_m^2 = 0$) and the lower (red) curve to $\sigma_m^2 = 0.5$. (c) Optimal phenotype determination when the maternal phenotype is a cue and there is a juvenile cue. Dashed curves show weights (β_J^*) given to the juvenile cue and solid curves show weights given to the maternal phenotype. Cases illustrated are: (i) $\sigma_J^2 = 1.0$, $\sigma_m^2 = 1.5$, (ii) $\sigma_J^2 = 1.0$, $\sigma_m^2 = 0$, (iii) $\sigma_J^2 = 2.5$, $\sigma_m^2 = 0$. In all figures, as λ increases σ is decreased so that the environmental variance if held fixed at the value Var(θ) = 2.5.

illustrating a certain lack of synergy between these cues. As λ increases the amount of phenotypic variation due to the influence of the genetic cue increases rapidly and that due to juvenile cue falls sharply. Further computation (not shown) reveals that the value of λ below which the genetic cue is ignored increases as the variance in the juvenile cue decreases.

Maternal phenotype as a cue

Since the reproductive success of the mother depends on the fit between her phenotype and the environment, the fact that an individual has been born suggests that her mother's phenotype was close to the environmental state. Thus, maternal phenotype can act as a selection-based source of information during development.

When the maternal phenotype is the only developmental cue, there is error-free transmission of information on the maternal phenotype to offspring ($\sigma_m^2 = 0$) and no developmental noise ($\delta = 0$), all phenotypes quickly reduce to $m = 0$ and the maternal phenotype becomes uninformative. Thus, in order that the maternal phenotype contains useful statistical information, it is necessary to include transmission error or developmental noise so as to maintain variation within a generation so that selection can act. This can be seen as a timescale issue; if there is no variation, the developmental system is committed to existing in a single phenotype, which is then an evolutionary dead end when the environment changes. By incorporting variation, the developmental system always ensures that at all future times, it is present in some individuals that do well.

As Fig. 4a shows, when variation is maintained the correlation between maternal phenotype and the environmental state increases with increasing λ, increasing the value, and hence the weight, put on the maternal phenotype as a cue, and less developmental noise is required (Fig. 4b). Transmission error perfectly substitutes for developmental noise, provided the variation generated by our chosen transmission error does not exceed that which is optimal (Fig. 4b). In all cases, fitness is a strictly increasing function of λ (Fig. 5b). Note that, unlike the model of Kuijper & Johnstone (2016), successive environments are always positively autocorrelated in our model so that we always have $\gamma^* \geq 0$.

As Fig. 4b illustrates, we always have $\delta^* > 0$ when $\sigma_m^2 = 0$. In particular, even though $\delta^* = 0$ when the phenotype is determined by $x = \delta\epsilon_\delta$ when $\mathrm{Var}(\theta) \leq 1$ (see above), we have $\delta^* > 0$ when phenotype determination is via $x = \gamma m + \delta\epsilon_\delta$; illustrating the synergy between noise and the influence of the maternal phenotype.

Maternal phenotype and juvenile cue: cross-generational environmental cue integration

We now consider the case where an individual can respond to the environmental cue during development (the juvenile cue)

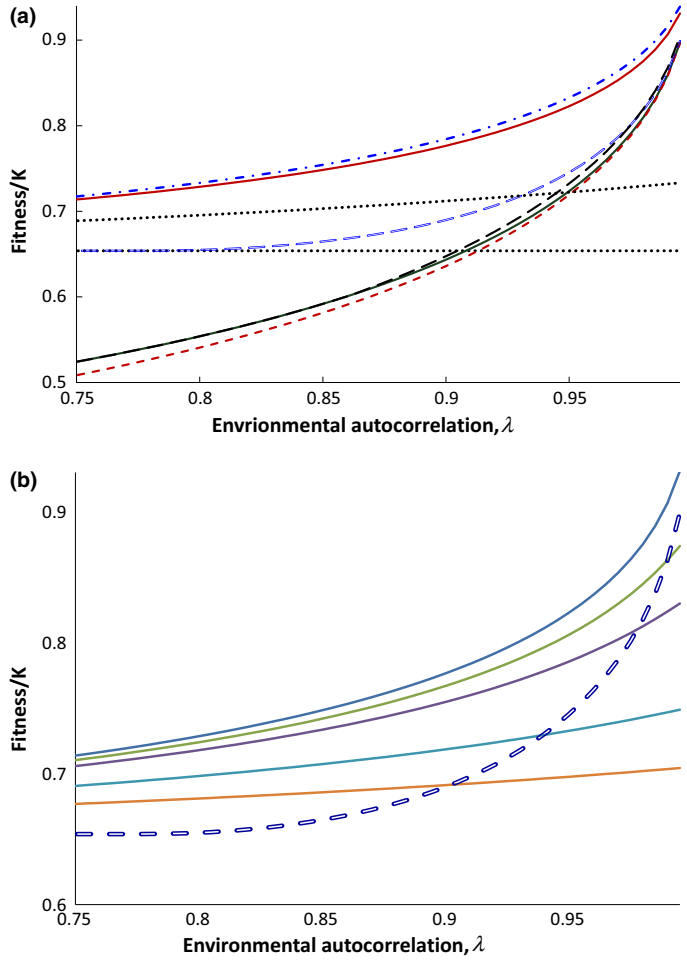

Figure 5 The fitness under optimal phenotype determination for various combinations of cues. (a) Dotted lines are top: juvenile cue + adult maternal cue, bottom: juvenile cue alone. Other curves are (from top to bottom): maternal phenotype + juvenile cue + adult maternal cue, maternal phenotype + juvenile cue, genetic cue + juvenile cue, maternal phenotype + genetic cue, maternal phenotype alone, genetic cue alone. $\sigma_m^2 = 0$ throughout. Random phenotype determination is allowed although $\delta^* = 0$ except for the maternal phenotype alone case. (b) Dashed curve is for the combination of the genetic cue and juvenile cue. Other curves are all for the combination of maternal cue and juvenile cue, with the error of transmission of the maternal cue (σ_m^2) increasing from top to bottom (cases shown, $\sigma_m^2 = 0, 0.1, 0.25, 1.0, 2.5$). In both figures, as λ increases σ is adjusted so that $\mathrm{Var}(\theta) = 2.5$. Juvenile cue error variance $\sigma_J^2 = 2.5$. Adult maternal cue error variance $\sigma_A = 2.5$.

and to the phenotype of her mother. It has previously been suggested that the maternal phenotype may encapsulate previous environmental cues (Townley & Ezard 2013; Kuijper & Hoyle 2015). To investigate this effect in this context and to motivate the form of trait determination, let c_0, c_{-1}, c_{-2}, ... be the juvenile cues received by the individual, her mother, her grandmother, and so on. During development, it would be clearly advantageous but not realistic for an individual to have available all the juvenile cues received by its ancestors. It might nevertheless be reasonable to assume some suitable summary of these past cues is passed on. To explore this idea, we note that in the absence of censoring (due to differential mortality), it is straightforward to show that the Bayes posterior mean of the current environmental state can be written as

$$\hat{c}_0 = (1-\kappa)[c_0 + \kappa\lambda c_{-1} + (\kappa\lambda)^2 c_{-2} + (\kappa\lambda)^3 c_{-3} + \cdots], \qquad (10)$$

where the constant κ is a function of λ, σ and σ_J (cf. Townley & Ezard 2013). This posterior mean is a sufficient statistic for the current environmental state, and can be written as follows: $\hat{c}_0 = (1-\kappa)c_0 + \kappa\lambda\hat{c}_{-1}$, where $\hat{c}_{-1}$ is the corresponding posterior mean for the mother. Assuming the phenotype determination satisfies $x = \hat{\beta}_J \hat{c}_0$, we can thus write this trait as $x = (1-\kappa)\hat{\beta}_J c_J + \kappa\lambda m$, where, in keeping with previous notation, we now denote the current juvenile cue c_0 by c_J and the phenotype of the mother by m. This analysis shows that if phenotype determination is of the form $x = \beta_J c_J + \gamma m$, then the maternal phenotype provides information in two different ways. As before, it provides selection-based information, but now that there is a juvenile cue, it also encapsulates information from previous juvenile cues. This increases the correlation between the maternal phenotype and the current environmental state (Fig. 4a), and hence increases the value of the maternal phenotype as a cue. Consequently, the maternal phenotype should always be used as a cue ($\gamma^* > 0$) when both are available (SI.9). This is in contrast to the combination of the maternal adult cue and the maternal phenotype, when it can be the case that $\gamma^* = 0$ (Uller *et al.* 2015).

As the environmental autocorrelation increases, the maternal phenotype becomes a more valuable cue because both the past selective environment has been more stable and because past juvenile cues are more relevant to current conditions. Thus, under optimal phenotype determination, more weight is given to the maternal phenotype as a cue and less to the current juvenile cue (Ezard *et al.* 2014; Uller *et al.* 2015), although relative weights depend on cue error variances and the fidelity in transmission of the maternal phenotype (Fig. 4c).

Comparison of genetic and maternal cues

Figure 5a illustrates how cues perform in combination. When the maternal phenotype is the only cue fitness is very similar to that when the genetics effect is the only cue (the maternal cue is slightly superior as it is transmitted to the offspring without error here, whereas the genetic effect mutates), so that the two cues are essentially interchangeable. Furthermore, very little is gained by allowing both cues at the same time. However, the situation is completely different when there is a juvenile environmental cue; the synergy between this cue and the maternal phenotype results in significantly higher fitness than the combination of juvenile cue and genetic cue, which have no synergy. Furthermore, the genetic effect is not used when this third cue is available in this setting. Adding the genetic effect to the other two cues is rarely advantageous, although its inclusion increases fitness slightly when there is developmental noise and λ is very close to 1 (not illustrated).

Adding noise to the transmission of the maternal phenotype reduces the advantage of the maternal cue and juvenile cue combination (Fig. 5b), but this combination remains superior to that of the genetic and environmental cue even when there is considerable noise unless the environmental autocorrelation is close to $\lambda = 1$.

The combination of juvenile and adult maternal environmental cues is inferior to the combination of juvenile and maternal phenotype (Fig. 5a) unless there is significant error in transmission of her phenotype (Fig. 5b), since the maternal phenotype encapsulates information on earlier environments. Furthermore adding the adult maternal cue to the juvenile and maternal phenotype only produced a small increase in fitness (Fig. 5a).

DISCUSSION

We allow the development of an individual to be affected by four cues. Two are directly observed environmental cues; a juvenile cue that the individual experienced during development and a cue experienced by her mother as an adult and passed on to the individual. Two are selection-based cues; a quantitative genetic effect and the phenotype of the mother. The three cues passed on from the mother use separate inheritance channels (Fig. 1) so as to give a clear separation of the effects of selection-based versus detection-based cues. Our main focus is on the interaction of the various cues, and how this depends on environmental variance and autocorrelation, the accuracy of environmental cues and the accuracy of transmission of the maternal phenotype. We give the first clear demonstration of the positive synergy between environmental cues and the maternal phenotype and lack of synergy between environmental cues and cue genes. In addition, we show that the juvenile cue can act as a randomisation device, analyse the feedback between use of a genetic cue and its value as a cue, and highlight issues of timescale. Table 1 summarises the relative influences of the cues that are predicted by our model.

When the environmental autocorrelation is low, the mature phenotype mainly depends on the juvenile cue since the maternal adult cue is out of date (Fig. 2a) and the selection-based cues are poorly correlated with the current environmental state (see e.g. Fig. 3a). There is a strong dependence on the juvenile cue if it is accurate, but even an inaccurate cue acts as a source of phenotype diversification and removes the need to bet hedge via developmental noise when the environmental variance is high. In our model, cues received by different population members are uncorrelated given the environment. For example, if the environmental state represented mean food availability, the actual amount found by different individuals might be centred on this mean but vary in an uncorrelated way due to good and bad luck when foraging. However, any cue, even if inaccurate, which gave a spread of estimates of the environmental state, could potentially obviate the need to have truly randomised phenotype determination; although noise in gene expression will inevitably introduce some randomisation in development (Eldar & Elowitz 2010).

When the environmental autocorrelation is high and there is high error in the transmission of the information on the maternal phenotype to offspring, the quantitative genetic effect is always used as a cue, although the relative weight put on this cue depends on both the strength of the autocorrelation and the accuracy of the two environmental cues.

The strength of selection on cue genes increases with their influence in development; a 'use it or lose it' principle that we demonstrate for the first time (Fig. 3a). This result relates to the finding of Kawecki (2000) that the effect of a modifier changes the selection on structural genes. Analogous feedback also occurs in models of phenotype determination in spatially heterogeneous environments. For example, if population members are natally philopatric then they tend to be born in local habitats to which they are already adapted, so that it can be optimal to be natally philopatric, ignoring developmental cues that have significant probability of error (McNamara & Dall 2011). If, however, population members took notice of such cues, they would disperse more and might not be particularly adapted to their birth habitat. It would then be better to take notice of developmental cues; i.e. not be natally philopatric. The presence of feedback raises the possibility that there may be more than one local fitness optima (Dall *et al.* 2015), although the fitness landscapes appears unimodal in the cases illustrated in Fig. 3.

When the environment is highly autocorrelated and there is high fidelity in the inheritance of information on the maternal phenotype, both genetic and maternal-phenotype selection-based cues act in a similar manner, and are alternative means of phenotype determination, when detection-based cues are inaccurate (Fig. 5a). However, these interact in very different ways with the detection-based environmental cues when the latter are accurate, since the maternal phenotype acts as a summary of previous detection-based cues (a sort of phenotypic memory sensu Kuijper & Johnstone (2016)). Consequently, the combination of environmental cue and maternal

Table 1 The combination of cues that is predicted under various combinations of factors (the degree of environmental autocorrelation, the accuracy of environmental cues and the accuracy with which the mother's phenotype can be passed to offspring)

Ecological conditions			Detection based		Selection based	
Env. autocorrelation	Env. cues	Phenotype inheritance	Juvenile cue	Adult cue	Maternal phenotype	Genes
Low	Any	Any	✓	×	×	×
High	Accurate	Very inaccurate	✓✓	✓✓	×	✓
High	Inaccurate	Very inaccurate	✓	✓	×	✓✓
High	Inaccurate	Accurate	✓	✓	××	✓ ✓
					✓✓	××
High	Accurate	Accurate	✓✓	✓✓	✓ ✓	×

A single tick denotes significant selection pressure to use a cue, a cross denotes very weak selection pressure, double ticks or crosses denote very strong or extremely weak pressure, respectively. Under the fourth condition there are two alternative best methods of phenotype determination; rely heavily on the maternal phenotype or rely on genes (but not both). Note that although the maternal phenotype is categorised as a selection-based cue, it can incorportate detection-based information (see text).

phenotype achieves greater fitness than the combination of environmental cue and genetic cue, provided that the maternal phenotype can be accurately passed on to offspring (Fig. 5a). In both our model and that of Rivoire & Leibler (2014), a juvenile cue influences the adult phenotype, which in turn is passed on to the offspring. This is essentially a form of Lamarckism (by which we mean the inheritance of detection-based cues). From our analysis, this model of transmission seems to be a very efficient way of integrating information, but real organisms might not have mechanisms that can achieve it with high accuracy (except for cultural inheritance), so Lamarckian effects could be limited by a noisy transmission of the maternal phenotype.

In contrast to the model of Rivoire & Leibler (2014), our model has several channels of transmission from parent to offspring (Fig. 1), for instance separate channels for quantitative genetic effects and adult cues. This often corresponds to biological reality, perhaps as a consequence of evolution latching on to different feasible implementations of transgenerational effects. For instance, a transfer of a substance from mother to offspring might be a mechanism that more readily evolves than an integration of adult cues into the hereditary material. Well-studied cases of such mechanisms include the 'egg foam factor' that plays a part in the determination of the gregarious morph of desert locusts (Miller *et al.* 2008), and α-Tocopherol (a vitamin E) inducing rotifer morphs by being transmitted to the offspring (Gilbert 2016).

We have not explicitly investigated the role that the strength of selection might play, but previous work has shown that selection-based cues become more informative as selection increases in strength (Leimar *et al.* 2006; Kuijper & Hoyle 2015), although in contrast, Uller *et al.* (2015) (eqn 2.21 and below) find that the inheritance of the maternal phenotype (through incomplete resetting of an epigenetic mark) is favoured when selection is weak. In our model, we take cue or transmission accuracy as a given parameter. Future work might consider the evolution of channel accuracy. This issue would be especially important when extending our analysis to the social transmission of information and in the more complex case of the transmission of multivariate maternal effects (Townley & Ezard 2013; Kuijper *et al.* 2014; Chevin & Lande 2015). Our model also does not take into account environmental changes during the lifetime of an organism (see, e.g. Nettle *et al.* 2013). An obvious extension would be to incorporate both changes between and within generations within the same model. In such a setting, information passed across generations would act as a Bayesian prior that would then be updated during the lifetime (Stamps & Frankenhuis 2016).

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AUTHOR CONTRIBUTIONS

Inspired by conversations with OL, JMM formulated the model (with modifications suggested by the other authors), performed the analyses and obtained the main results. All authors contributed to the literature search and writing of the manuscript.

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